Clinical trial results:
A Phase 2a, Open-Label, Single Ascending Dose Study to Evaluate the Pharmacokinetics and Safety of Solriamfetol in Pediatric Participants with Narcolepsy

Summary

EudraCT number	2019-003008-11
Trial protocol	BE FR NL IT
Global end of trial date	04 February 2022

Results information

Result version number	v1 (current)
This version publication date	20 August 2022
First version publication date	20 August 2022

Trial information

Trial identification

Sponsor protocol code	JZP865-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Jazz Pharmaceuticals, Inc.
Sponsor organisation address	3170 Porter Drive, Palo Alto, United States, 94304
Public contact	Director, Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals, Inc., 1 215-832-3750, ClinicalTrialDisclosure@jazzpharma.com
Scientific contact	Director, Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals, Inc., 1 215-832-3750, ClinicalTrialDisclosure@jazzpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002184-PIP01-17
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy in improving wakefulness in pediatric participants with narcolepsy and to characterize the PK of single doses of solriamfetol in pediatric participants with narcolepsy.

Protection of trial subjects:

The study will be conducted in accordance with applicable local regulations relating to GCP and with the SOPs of the CRO or Jazz Pharmaceuticals, as applicable. These standards respect the following guidelines or laws:

- Guideline for GCP E6 (R2): ICH, November 2016.
- Good Clinical Practice Directive 205/28/EC.
- Clinical Trials Directive (European Medicines Agency [EMA]) Directive 2001/20/EC, as replaced by the EU Clinical Trials Regulation 536/2014 when it comes into application.

Endorsement of the ethical principles embedded in the above guidances and regulations ensures that the rights, safety and well-being of study participants are protected and are consistent with the principles that have their origin in the Declaration of Helsinki, World Medical Association –"Ethical Principles for Medical Research Involving Human Participants".

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	14
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	7
Adolescents (12-17 years)	7
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 12 pediatric participants who satisfied all eligibility criteria, 6 participants in each age group (Group 1: adolescents 12 to < 18 years old; Group 2: children 6 to < 12 years old), received solriamfetol over three treatment periods.

Pre-assignment

Screening details:

The study had a Screening Period for up to 28 days, 3 Treatment Periods during which participants were administered ascending doses of study intervention, and an End of Study Period to collect final safety evaluations. Periods 1, 2, and 3 were separated by a washout of 14 ± 2 days. Dose was escalated only if the previous dose was tolerated.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Group 1: 12 to <18 years old

Arm description:

Participants ages 12 to <18 years old were administered a single oral dose (75 mg) of solriamfetol.

Arm type	Experimental
Investigational medicinal product name	solriamfetol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each participant in Group 1 (12 to < 18 years old) period 1 received a single oral dose of 75 mg solriamfetol.

Arm title	Group 2: 6 to <12 years old

Arm description:

Participants ages 6 to <12 years old were administered a single oral dose (37.5 mg) of solriamfetol.

Arm type	Experimental
Investigational medicinal product name	solriamfetol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each participant in Group 2 (6 to < 12 years old) period 1 received a single oral dose of 37.5 mg solriamfetol.

Number of subjects in period 1	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Started	6	6
Completed	6	6

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Group 1: 12 to <18 years old

Arm description:

Participants ages 12 to <18 years old were administered a single oral dose (150 mg) of solriamfetol.

Arm type	Experimental
Investigational medicinal product name	solriamfetol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each participant in Group 1 (12 to < 18 years old) period 2 received a single oral dose of 150 mg solriamfetol.

Arm title	Group 2: 6 to <12 years old

Arm description:

Participants ages 6 to <12 years old were administered a single oral dose (75 mg) of solriamfetol.

Arm type	Experimental
Investigational medicinal product name	solriamfetol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each participant in Group 2 (6 to < 12 years old) period 2 received a single oral dose of 75 mg solriamfetol.

Number of subjects in period 2	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Started	6	6
Completed	6	6

Period 3

Period 3 title	Period 3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Group 1: 12 to <18 years old

Arm description:

Participants ages 12 to <18 years old were administered a single oral dose (300 mg) of solriamfetol.

Arm type	Experimental
Investigational medicinal product name	solriamfetol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each participant in Group 1 (12 to < 18 years old) period 3 received a single oral dose of 300 mg solriamfetol.

Arm title	Group 2: 6 to <12 years old

Arm description:

Participants ages 6 to <12 years old were administered a single oral dose (150 mg) of solriamfetol.

Arm type	Experimental
Investigational medicinal product name	solriamfetol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each participant in Group 2 (6 to < 12 years old) period 3 received a single oral dose of 150 mg solriamfetol.

Number of subjects in period 3	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Started	6	6
Completed	6	6

Baseline characteristics

Reporting groups[1]	
Reporting group title	Group 1: 12 to <18 years old
Reporting group description:	
Participants ages 12 to <18 years old were administered a single oral dose (75 mg) of solriamfetol.	
Reporting group title	Group 2: 6 to <12 years old
Reporting group description:	
Participants ages 6 to <12 years old were administered a single oral dose (37.5 mg) of solriamfetol.	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: Fourteen potential participants were screened for this study; 2 failed to meet all entry criteria. A total of 12 participants were enrolled and dosed from 4 centers in the EU (France, Belgium, and Italy), and all 12 participants completed the study.

Reporting group values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Total
Number of subjects	6	6	12
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	6	6
Adolescents (12-17 years)	6	0	6
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	15.612	9.862	
standard deviation	± 1.2988	± 1.5508	-
Gender categorical Units: Subjects			
Female	3	4	7
Male	3	2	5

End points

End points reporting groups

Reporting group title	Group 1: 12 to <18 years old
Reporting group description:	
Participants ages 12 to <18 years old were administered a single oral dose (75 mg) of solriamfetol.	
Reporting group title	Group 2: 6 to <12 years old
Reporting group description:	
Participants ages 6 to <12 years old were administered a single oral dose (37.5 mg) of solriamfetol.	
Reporting group title	Group 1: 12 to <18 years old
Reporting group description:	
Participants ages 12 to <18 years old were administered a single oral dose (150 mg) of solriamfetol.	
Reporting group title	Group 2: 6 to <12 years old
Reporting group description:	
Participants ages 6 to <12 years old were administered a single oral dose (75 mg) of solriamfetol.	
Reporting group title	Group 1: 12 to <18 years old
Reporting group description:	
Participants ages 12 to <18 years old were administered a single oral dose (300 mg) of solriamfetol.	
Reporting group title	Group 2: 6 to <12 years old
Reporting group description:	
Participants ages 6 to <12 years old were administered a single oral dose (150 mg) of solriamfetol.	

Primary: Change in Pictorial Sleepiness Scale (PSS) Score from Day 1 Predose to Time of Individual Tmax Postdose for Each Period

End point title	Change in Pictorial Sleepiness Scale (PSS) Score from Day 1 Predose to Time of Individual Tmax Postdose for Each Period[1]

End point description:

The PSS is a pictorial scale used to measure instantaneous perceived sleepiness. The assessment consists of 5 cartoon faces depicting increasing degrees of sleepiness. For each assessment, the faces were presented to the participant in a random 2-dimensional array, and participants chose the face that best describes how sleepy or alert they feel at that time. Each response was converted to a numerical ranked score. PSS is presented on a scale of 0 to 5.58, with 0 corresponding to the most alert, and 5.58 corresponding to the most sleepy. Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3 for the last participant in Group 1.

End point type	Primary

End point timeframe:

Day 1 predose to time of individual Tmax postdose.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	5	0[3]	5
Units: Score on a scale				
arithmetic mean (standard deviation)	()	0.000 (± 1.1809)	()	-1.450 (± 1.6088)

Notes:

[2] - Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3 .

[3] - Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	5		
Units: Score on a scale				
arithmetic mean (standard deviation)	-3.860 (± 0)	-0.708 (± 0.6463)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Global Impression of Change (CGIc) Score on Day 1 Relative to Day -1 for Each Period

End point title	Clinical Global Impression of Change (CGIc) Score on Day 1 Relative to Day -1 for Each Period[4]

End point description:

The CGIc is a 5-point Likert-type rating scale widely used to assess efficacy in clinical studies. For each period, investigators will rate their impression of any change in the participant's overall sleepiness on dosing day compared to overall baseline (Day 1) sleepiness. The questionnaire is rated on a 5-point scale: 1=Much improved, 2=Minimally improved, 3=No change, 4=Minimally worse, 5=Much worse. Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3 for the last participant in Group 1.

End point type	Primary

End point timeframe:

10 hours postdose.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	5	0[6]	5
Units: Score on a Scale				
arithmetic mean (standard deviation)	()	2.2 (± 0.45)	()	1.2 (± 0.45)

Notes:

[5] - Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3.

[6] - Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	5		
Units: Score on a Scale				
arithmetic mean (standard deviation)	1.0 (± 0)	1.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax)

End point title	Maximum Plasma Concentration (Cmax)[7]

End point description:

Descriptive statistics were used to summarize pharmacokinetic (PK) parameters by dose and age group, as appropriate.

End point type	Primary

End point timeframe:

Day 1 predose up to 10 hours postdose.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ng/mL				
arithmetic mean (standard deviation)	385.0 (± 76.98)	355.7 (± 144.1)	811.5 (± 148.9)	673.8 (± 285.5)

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ng/mL				
arithmetic mean (standard deviation)	1525 (± 375.9)	1350 (± 610.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve from Time 0 to the Time t of the Last Quantifiable Concentration (AUC0-t)

End point title	Area Under the Plasma Concentration-Time Curve from Time 0 to the Time t of the Last Quantifiable Concentration (AUC0-t)[8]

End point description:

Descriptive statistics were used to summarize pharmacokinetic (PK) parameters by dose and age group,

as appropriate.

End point type	Primary

End point timeframe:

Day 1 predose up to 10 hours postdose.

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ng*h/mL				
arithmetic mean (standard deviation)	2588 (± 586.6)	1701 (± 534.3)	5410 (± 986.2)	3687 (± 1333)

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ng*h/mL				
arithmetic mean (standard deviation)	10800 (± 1949)	7623 (± 2831)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve from Time 0 to Infinity (AUC0-inf)

End point title	Area Under the Plasma Concentration-Time Curve from Time 0 to Infinity (AUC0-inf)[9]

End point description:

Descriptive statistics were used to summarize pharmacokinetic (PK) parameters by dose and age group, as appropriate.

End point type	Primary

End point timeframe:

Day 1 predose up to 10 hours postdose.

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[10]	4	0[11]	0[12]
Units: ng*h/mL				
arithmetic mean (standard deviation)	()	2204 (± 691.5)	()	()

Notes:

[10] - Due to limited sampling, estimation of AUC 0-inf was limited across the dose levels.

[11] - Due to limited sampling, estimation of AUC 0-inf was limited across the dose levels.

[12] - Due to limited sampling, estimation of AUC 0-inf was limited across the dose levels.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	0[14]		
Units: ng*h/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[13] - Due to limited sampling, estimation of AUC 0-inf was limited across the dose levels.

[14] - Due to limited sampling, estimation of AUC 0-inf was limited across the dose levels.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Cmax (tmax)

End point title	Time to Reach Cmax (tmax)[15]

End point description:

Descriptive statistics were used to summarize pharmacokinetic (PK) parameters by dose and age group, as appropriate.

End point type	Primary

End point timeframe:

Day 1 predose up to 10 hours postdose.

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hours				
median (full range (min-max))	2.54 (2.00 to 3.08)	1.52 (0.98 to 3.00)	1.02 (0.97 to 3.03)	2.53 (2.00 to 3.00)

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hours				
median (full range (min-max))	2.56 (1.00 to	1.52 (1.00 to		

6.02)	2.97)

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Terminal Elimination Half-Life (t½)

End point title	Apparent Terminal Elimination Half-Life (t½)[16]

End point description:

Descriptive statistics were used to summarize pharmacokinetic (PK) parameters by dose and age group, as appropriate.

End point type	Primary

End point timeframe:

Day 1 predose up to 10 hours postdose.

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: hours				
arithmetic mean (standard deviation)	9.060 (± 4.411)	4.060 (± 0.6336)	9.583 (± 3.354)	4.612 (± 0.6538)

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: hours				
arithmetic mean (standard deviation)	9.820 (± 5.485)	4.704 (± 1.262)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL/F)

End point title	Apparent Oral Clearance (CL/F)[17]

End point description:

Descriptive statistics were used to summarize pharmacokinetic (PK) parameters by dose and age group, as appropriate.

End point type	Primary

End point timeframe:

Day 1 predose up to 10 hours postdose.

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[18]	4	0[19]	0[20]
Units: L/h				
arithmetic mean (standard deviation)	()	18.16 (± 4.961)	()	()

Notes:

[18] - Due to limited sampling, estimation of CL/F was limited across the dose levels.

[19] - Due to limited sampling, estimation of CL/F was limited across the dose levels.

[20] - Due to limited sampling, estimation of CL/F was limited across the dose levels.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[21]	0[22]		
Units: L/h				
arithmetic mean (standard deviation)	()	()		

Notes:

[21] - Due to limited sampling, estimation of CL/F was limited across the dose levels.

[22] - Due to limited sampling, estimation of CL/F was limited across the dose levels.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (Vd/F)

End point title	Apparent Volume of Distribution (Vd/F)[23]

End point description:

Descriptive statistics were used to summarize pharmacokinetic (PK) parameters by dose and age group, as appropriate.

End point type	Primary

End point timeframe:

Day 1 predose up to 10 hours postdose.

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[24]	4	0[25]	0[26]
Units: Liters				
arithmetic mean (standard deviation)	()	97.39 (± 30.24)	()	()

Notes:

[24] - Due to limited sampling, estimation of Vz/F was limited across the dose levels.

[25] - Due to limited sampling, estimation of Vz/F was limited across the dose levels.

[26] - Due to limited sampling, estimation of Vz/F was limited across the dose levels.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[27]	0[28]		
Units: Liters				
arithmetic mean (standard deviation)	()	()		

Notes:

[27] - Due to limited sampling, estimation of Vz/F was limited across the dose levels.

[28] - Due to limited sampling, estimation of Vz/F was limited across the dose levels.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Pictorial Sleepiness Scale (PSS) Score from Day 1 Predose to 1, 2, 3, 4, 6, 8, and 10 Hours Postdose for Each Period

End point title	Change in Pictorial Sleepiness Scale (PSS) Score from Day 1 Predose to 1, 2, 3, 4, 6, 8, and 10 Hours Postdose for Each Period[29]

End point description:

The PSS is a pictorial scale used to measure instantaneous perceived sleepiness. The assessment consists of 5 cartoon faces depicting increasing degrees of sleepiness. For each assessment, the faces were presented to the participant in a random 2-dimensional array, and participants chose the face that best describes how sleepy or alert they feel at that time. Each response was converted to a numerical ranked score. PSS is presented on a scale of 0 to 5.58, with 0 corresponding to the most alert, and 5.58 corresponding to the most sleepy. Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3 for the last participant in Group 1.

End point type	Secondary

End point timeframe:

Day 1 predose to 1, 2, 3, 4, 6, 8, and 10 hours postdose.

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point.

End point values	Group 2: 6 to <12 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	1	5
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Predose	1.002 (± 0.9147)	2.118 (± 2.0660)	3.860 (± 0)	1.710 (± 1.5610)
CFB to 1 hour postdose	0.236 (± 1.2934)	-1.784 (± 1.3912)	-3.860 (± 0)	-0.374 (± 1.2517)
CFB to 2 hours postdose	0.104 (± 1.3721)	-0.334 (± 0.7468)	-3.860 (± 0)	-0.472 (± 2.1164)
CFB to 3 hours postdose	0.236 (± 1.2934)	-1.784 (± 1.3912)	-3.860 (± 0)	-1.376 (± 1.4292)
CFB to 4 hours postdose	0.000 (± 1.6700)	-1.784 (± 1.3912)	-3.860 (± 0)	-1.042 (± 1.9363)

CFB to 6 hours postdose	1.244 (± 1.9701)	-1.784 (± 1.3912)	-3.860 (± 0)	-0.472 (± 1.6726)
CFB to 8 hours postdose	0.000 (± 1.1809)	-1.450 (± 1.6088)	-3.860 (± 0)	-0.138 (± 1.7467)
CFB to 10 hours postdose	-0.098 (± 1.0165)	-1.784 (± 1.3912)	-3.860 (± 0)	-0.708 (± 1.6726)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a CGIc of "Much Improved" or "Minimally Improved" on Day 1 Relative to Day -1 for Each Period

End point title	Percentage of Participants with a CGIc of "Much Improved" or "Minimally Improved" on Day 1 Relative to Day -1 for Each Period

End point description:

The CGIc is a 5-point Likert-type rating scale widely used to assess efficacy in clinical studies. For each period, investigators will rate their impression of any change in the participant's overall sleepiness on dosing day compared to overall baseline (Day 1) sleepiness. The questionnaire is rated on a 5-point scale: 1=Much improved, 2=Minimally improved, 3=No change, 4=Minimally worse, 5=Much worse. Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3 for the last participant in Group 1.

End point type	Secondary

End point timeframe:

Day 1 predose up to 10 hours postdose.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[30]	5	0[31]	5
Units: participants				
Much improved		0		4
Minimally improved		4		1

Notes:

[30] - Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3.

[31] - Data for Group 1 are not shown, as efficacy assessments were not implemented until Period 3.

End point values	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	5		
Units: participants				
Much improved	1	5		
Minimally improved	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the time written informed consent is obtained until the End of Study Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Group 1: 12 to <18 years old

Reporting group description:

Participants ages 12 to <18 years old were administered 3 single oral doses (75 mg, 150 mg, 300 mg) of solriamfetol (if tolerated) during 3 separate periods, in an ascending manner.

Reporting group title	Group 2: 6 to <12 years old

Reporting group description:

Participants ages 6 to <12 years old were administered 3 single oral doses (75 mg, 150 mg, 300 mg) of solriamfetol (if tolerated) during 3 separate periods, in an ascending manner.

Serious adverse events	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Group 1: 12 to <18 years old	Group 2: 6 to <12 years old	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	1 / 6 (16.67%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	2	0	

Headache subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Infections and infestations Asymptomatic COVID-19 subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2020	The primary reason for Amendment 1 was to correct/clarify the clinical laboratory tests to be performed and update the list of analytes evaluated at the urine drug screen. Changes also were made for clarity regarding timing of standard meals/snacks. An editorial change was made to reflect the approval status for solriamfetol in the European Union.
10 January 2021	The primary reason for this global amendment was to add a primary efficacy objective and corresponding endpoints, which elevates the study from phase 1 to phase 2a. To reflect the change in study phase, the study title was also updated. A primary efficacy objective and associated primary and secondary efficacy endpoints were added to enable preliminary efficacy evaluation; added all endpoints to this section for clarity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

One participant had a single dose delayed (out-of-window Visit 3) due to COVID-19 resulting in an extended washout between Periods 2 and 3. This did not negatively impact the safety of the participant, or the integrity of the PK or safety data.

Notes: